UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

MJ

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/226,794	01/07/99	DEBINSKI W	6460-4

HM22/0522

J RODMAN STEELE JR
QUARLES AND BRADY
222 LAKEVIEW AVENUE SUITE 400
P O BOX 3188
WEST PALM BEACH FL 33402-3188

EXAMINER	
UNGAR, S	
ART UNIT	**PAPER NUMBER**
1642	9

DATE MAILED: 05/22/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/226,794	Debrinski et al
Examiner	**Group Art Unit**
Ungar	1642

☒ Responsive to communication(s) filed on *Mar 1, 2000*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-13* is/are pending in the application.

Of the above, claim(s) *7-13* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-6* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

1. The Election filed March 1, 2000 (Paper No. 8) in response to the Office Action of January 3, 2000 (Paper No. 6) is acknowledged and has been entered. Claims 1-13 are pending in the application and Claims 7-13 have been withdrawn from further consideration by the examiner under 37 CAR 1.142(b) as being drawn to non-elected inventions. Claims 1-6 are currently under prosecution.

2. Applicant's election with traverse of Group I, claims 1-6 and Applicant's election of the species of rate of tumor growth inhibited, in Paper No. 8 is acknowledged. The traversal is on the ground(s) that the inventions have not been shown to be distinct since Groups I-IV relate to IL13 receptors. The argument drawn to the restriction of the Groups has been considered but has not been found persuasive because the inventions were shown to be distinct for the reasons set forth in Paper No. 6. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL. Applicant has admitted on the record that the species are obvious variants, one over the other, and therefore the requirement for election of species is withdrawn.

Claim Rejections - Double Patenting

3. The non-statutory double patenting rejection, whether of the obviousness type or non-obviousness type, is based on a judicially created doctrine grounded in public policy (a policy relected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ

438, 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CAR 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CAR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed b the assignee must fully comply with 37 CAR 3.73(b).

4. Claims 1 and 3-5 are rejected under the judicially created doctrine of obviousness-type double patenting as unpatentable over claims 14 and 16-20 of US Patent No. 5,614,191, IDS item.

. Although the conflicting claims are not identical, they are not patentably distinct from each other because they relate to the same inventive concept. The instant claims are generic to the claims of the patent and would have been obvious in view of the patented claims which have all of the characteristics of a method of reducing the rate of growth of tumor cells *in vivo* (claim 20) wherein the tumor cells comprise an IL13-specific receptor comprising delivering into the subject a molecule having an IL13 moiety and a cytotoxic moiety in an amount effective to reduce the rate of growth of tumor cells (claims 14 and 16-19). Although the claims are not specifically drawn to the limitations "wherein the rate of the tumor growth is reduced by at least 25%", "wherein tumor volume is reduced", since the method of

the patent comprises the same method steps as claimed in the instant invention, that is, administering a molecule comprising an IL13-moiety and a cytotoxin to a mammalian subject with the same population of cells, the claimed method is anticipated and obvious and will inherently lead to at least a 25% reduction in tumor growth and will inherently lead to a reduction in tumor volume.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

6. Claim 3 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is confusing because it recites the phrase "the rate of tumor growth is reduced by at least 25%". The claim is confusing because it is not clear to what the reduced rate is compared.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 1 and 3-5 are rejected under 35 U.S.C. § 102(b) as being anticipated by US Patent No. 5,614,191 (IDS item).

The claims are drawn to a method of reducing the rate of growth of tumor cells *in vivo* wherein the tumor cells comprise an IL13-specific receptor comprising delivering into the subject a molecule having an IL13 moiety and a cytotoxic moiety in an amount effect to reduce the rate of growth of tumor cells wherein the rate of the tumor growth is reduced by at least 25%, wherein tumor volume is reduced.

US Patent No. 5,614, 191 teaches a method of impairing growth of a solid tumor cell bearing an IL-13 receptor comprising contacting said tumor cell with a molecule comprising an effector molecule attached to IL-13, wherein the effector molecule is a cytotoxin (claims 14 and 16-19), PE38QQR (see Example 4, col 21-col 22), wherein said tumor cell growth is tumor cell growth in a human (claim 20). Since the method of the prior art comprises the same method steps as claimed in the instant invention, that is, administering a molecule comprising an IL13-moiety and a cytotoxin to a mammalian subject with the same population of cells, the claimed method is anticipated because the method will inherently lead to at least a 25%

reduction in tumor growth and will inherently lead to a reduction in tumor volume.. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

9. Claims 1-5 are rejected under 35 U.S.C. § 102(a) as being anticipated by Debinski et al (Abstract, The Society for Neuro-Oncology, 1998, San Francisco, CA, IDS item) as evidenced by Lopes et al (Mol. Chem. Neuropathyol., 1992, 17:273-287).

The claims are drawn to a method of reducing the rate of growth of tumor cells in vivo wherein the tumor cells comprise an IL13-specific receptor, wherein the tumor cells are glioblastoma multiforme cells, comprising delivering into the subject a molecule having an IL13 moiety and a cytotoxic moiety in an amount effective to reduce the rate of growth of tumor cells wherein the rate of the tumor growth is reduced by at least 25%, wherein the tumor volume is reduced.

Lopes et al teach that U-251 MG is a human glioblastoma multiforme cell line (see abstract).

Debinski et al teach administration of hIL-13 based cytotoxins which cured 25 to 40% of SCID mice bearing intracranial U-251 MG glioma xenografts. The reference further teaches that the majority of human glioblastoma cell lines over-express large numbers of receptor for IL13 and that the results in SCID mice provide unequivocal support for the restrictive hIL13R being the marker of GBM and finally teach that the marker can serve for the delivery of anti-GBM therapies. It is clear that since the tumors were cured, growth of the tumor was reduced by at least 25%. Since the method of the prior art comprises the same method steps as claimed in the instant invention, that is, administering a molecule comprising an

IL13-moiety and a cytotoxin to a mammalian subject with the same population of cells, the claimed method is anticipated because the method will inherently lead to a reduction in tumor volume.. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

11. Claims 1 and 6 are rejected under 35 U.S.C. § 103 as being unpatentable over US Patent No. 5,614,191 or Debinski et al (*Supra*).

The claims are drawn to a method of reducing the rate of growth of tumor cells *in vivo* wherein the tumor cells comprise an IL13-specific receptor comprising delivering into the subject a molecule having an IL13 moiety and a cytotoxic moiety wherein the delivering is by intratumoral injection.

US Patent No. 5,614,191 and Debinski et al teach as set forth above but do not teach a method wherein the molecule is delivered by intratumoral injection.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made o administer the molecule intratumorally because intratumoral injection of therapeutics was conventional in the art at the time the invention was made. One of ordinary skill in the art would have been motivated to intratumorally inject the molecule in order to avoid the problems associated with, for example, intravenous administration, which results in not only the dilution of the therapeutic but also renders it highly vulnerable to attack by the immune system.

12. Claims 1-5 are rejected under 35 U.S.C. § 103 as being unpatentable over US Patent No. 5,614,191 in view of Debinski et al (JBC, 1996, 271:22428-22433).

The claims are drawn to a method of reducing the rate of growth of tumor cells *in vivo* wherein the tumor cells comprise an IL13-specific receptor, wherein the tumor cells are glioblastoma multiforme cells, comprising delivering into the subject a molecule having an IL13 moiety and a cytotoxic moiety in an amount effective to reduce the rate of growth of tumor cells wherein the rate of the tumor growth is reduced by at least 25%, wherein the tumor volume is reduced.

US Patent No. 5,614,191 teach as set forth above but do not teach a method of treatment wherein the tumor cells to be treated are glioblastoma multiform cells.

Debinski et al teach that human glioblastoma multiforme explant cells are extremely sensitive to a chimeric protein composed of hIL13 and a cytotoxin, PE38QQR (see Abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use the method of US Patent No. 5,615,191 to treat a human patient with human glioblastoma multiforme tumor cells because Debinski et al teach that primary human glioblastoma multiforme cells are extremely sensitive to a chimeric protein composed of hIL13 and PE38QQR which appears to be the same construct used in the method of US Patent No. 5,615,191. One of ordinary skill in the art would have been motivated to use the method of US Patent No. 5,615,191 to treat a human patient with human glioblastoma multiforme tumor cells because US Patent No. 5,6615,191 specifically claims a method of impairing growth of a solid tumor cell bearing an IL-13 receptor and because Debinski et al have clearly taught that human glioblastoma multiforme cells are sensitive to and bind an IL13 construct and therefore would be expected to express hIL13 receptor.

12. No claims allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995. The fax phone number for this Art Unit is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar, PhD
Primary Patent Examiner
May 16, 2000